Supplemental material

APPENDIX 8: Ethically defensible plan

Determination of findings that will be returned and actions (*National Statement* Guidelines 3.3.36, 3.3.43, 3.3.44)

Only P/LP variants in known CPGs are considered reportable, and results will be distributed to the treating oncologist in the form of a report, if consent for return of results is obtained. The report will contain a summary and interpretation of laboratory results, a determination that the variant is inherited or de novo (where possible), and a recommendation for genetic counselling referral based on the reportable findings and/or reported clinical/family history features. Ethically approved, patient-friendly leaflets will accompany the report to facilitate results discussions. A multi-pronged approach mitigating the risk of revealing incidental findings (IF) will be implemented, however, reportability will be reviewed on a case-by-case basis if an IF is identified considered clinically actionable during childhood. Where reported, referral will be made to the local genetics service for genetic counselling and management of the condition identified.

Validation and assessment of findings (*National Statement* Guidelines 3.3.45 and 3.3.46)

Genomics and multidisciplinary clinical teams will review the variants via a three-step pathway. Variants can be reclassified over time, and this will be periodically reviewed, and a new report will be issued as required. The result report will clearly state the findings were generated as part of the research, and clinical confirmation of reportable variants in an accredited laboratory is necessary before any changes in clinical management. The study team encourages PREDICT results to be delivered in a joint appointment with the treating clinician and a study genetic counsellor.

Consent to disclosure of findings and notification requirements (*National Statement* Guidelines 3.3.47– 3.3.57)

To facilitate the involvement of the child or adolescent in the pre-test consent discussion, age-appropriate patient information sheets have been developed. A two-step consent process will be implemented, including (1) preliminary discussion regarding the study aims and requirements of participation, followed by the offer of further discussion with the study genetic counsellor (strongly encouraged in certain scenarios including significant distress, limited health literacy, or where there are differing preferences between family member participants); and (2) the consent form is reviewed between the treating clinician and/or study genetic counsellor and the participating family. All attempts will be made to re-consent participants upon reaching the age of majority during the study at their next scheduled visit if they have not previously consented for themselves. The decision for individuals declining return of results will not be routinely checked (as per *National Statement* guideline 3.3.53). However, families will be made aware during the pre-test discussion that they can update their decision at any time during the study and will be provided with study contact details to facilitate this. Special considerations for disclosing findings and other correspondence regarding the study will be made for bereaved families. Requests for the return of raw data and/or biospecimens will be facilitated, where possible.

Fuentes Bolanos NA, *et al. BMJ Open* 2023; 13:e070082. doi: 10.1136/bmjopen-2022-070082